REMARKS

Applicants have studied the Office Action, and have amended the claims in response thereto. It is respectfully submitted that the application, as amended, is in condition for allowance. Prior to entry of the present amendment, claims 32-52 were pending in the present application. Claims 40-44 have been canceled by virtue of the present amendment; claims 1-31 having been previously canceled. Claims 32 and 45 have been amended. No new matter has been added. Reconsideration and allowance of the claims in view of the foregoing amendment and the ensuing remarks are respectfully requested.

Claim 32 has been amended to more particularly describe that which Applicants consider to be their invention. As amended, claim 32 describes *"[a] method of inhibiting neoplastic cellular proliferation or transformation, or both,* in vitro.*"* Furthermore, the method includes *"delivering to [a] mammalian cell a composition comprising an expression vector comprising a promoter and a polynucleotide, said polynucleotide comprising a first DNA segment encoding a mammalian PTTG2 peptide consisting of amino acid residues 1-191 of SEQ ID NO:64."* Support for these amendments may be found throughout the Specification; for example, at page 15, lines 8-16, and at page 27, lines 16-26.

Claim 45 has been amended to more particularly describe that which Applicants consider to be their invention. As amended, claim 45 describes *"[a] mammalian cell maintained* in vitro *that endogenously overexpresses PTTG1, and in which neoplastic cellular proliferation or transformation, or both, is inhibited."* The inventive cell includes *"a composition comprising an expression vector comprising a promoter and a polynucleotide, said polynucleotide comprising a first DNA segment encoding a mammalian PTTG2 peptide consisting of amino acid residues 1-191 of SEQ ID NO:64."* Support for these amendments may be found throughout the Specification; for example, at page 15, lines 8-16, at page 27, lines 16-26, and at page 57, lines 18-26.

In the Office Action, Examiner acknowledged Applicants' claim for domestic priority under 35 U.S.C. § 119(e) and 120, and further noted that *"the provisional application 60/031,338 and applications 09/777,422, 09/730,469, 09/687,911, 09/569,956, 08/894,251 and PCT/US97/21463*

fail to disclose the nucleotide sequence of SEQ ID No. 63 and the amino acid sequence of SEQ ID No. 64." Examiner thus denied the benefits of these applications, and indicated that *"[t]he effective filing date of the present application is the actual filing date 5-11-01."*

Applicants respectfully, yet strongly disagree with Examiner's conclusion regarding their priority claim. In any event, unless Examiner can identify a reference upon which to base a rejection that calls into question Applicants' entitlement to their priority claim, Applicants further respectfully submit that this issue is purely an academic matter, and is of no moment to the patentability of their invention, as presently claimed.

In the Office Action, Examiner advised Applicants that, *"should claims 40-44 be found allowable, claims 45 and 48-51 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof."* Claims 40-44 have been canceled by virtue of the present amendment. Applicants therefore respectfully submit that this potential objection has been obviated.

In the Office Action, Examiner rejected claims 32-52 under 35 U.S.C. § 101 as lacking utility; particularly, *"because . . . [t]here is no specific utility or a well-established utility for the mammalian cells whose neoplastic cellular proliferation or transformation, or both, is inhibited, or for the method of producing said mammalian cells in vitro."* Examiner further noted that *"[t]he only readily apparent use for the method is to study the effects of the method,"* and that *"[t]he use of an invention as an object of further research or study does not meet the requirement of 35 U.S.C. 101."* With respect to claims 40-44, which have been canceled by virtue of the present amendment, this rejection is rendered moot. With respect to the remaining claims, this rejection is respectfully traversed.

To satisfy the utility requirement of 35 U.S.C. § 101, a claimed invention must have either a well-established utility or a credible "specific and substantial utility" that is asserted by the applicant. MPEP § 2107(II). Where a claimed invention has a well-established utility, *"rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, based on lack of utility should not be imposed."* MPEP § 2107.02(II)(B) (citing In re Folkers, 344 F.2d 970 (CCPA 1965)). In the absence of a well-established utility, the applicant should assert a specific and substantial utility. MPEP §

2107.02(II)(A). Moreover, *"[i]n most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. § 101."* MPEP § 2107.02(III)(A). The burden is on the Office to make a *prima facie* showing that a claimed invention lacks utility, and a sufficient evidentiary basis for factual assumptions relied upon in establishing this *prima facie* showing must be provided. MPEP § 2107.02(IV) (citing *In re Gaubert*, 524 F.2d 1222, 1224 (CCPA 1975)). Furthermore, with respect to substantial utility, *"[u]tilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities."* However, *"[a]n assessment that focuses on whether an invention is useful only in a research setting . . . does not address whether the invention is in fact 'useful' in a patent sense . . . Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm"* (emphasis added). MPEP § 2107.01(I).

Applicants' claimed invention relates to a method for inhibiting neoplastic cellular proliferation and/or transformation in mammalian cells *in vitro*, as well as mammalian cells that are modified to possess these biological characteristics. Modified cells and the method used to prepare them have a number of well-established utilities that will be readily recognized by those of skill in the art. By way of example, such modified cells can be used to screen pharmacological agents by routine procedures in order to assess the agents' ability to modulate tumorigenesis. Alternatively, the inventive cells can be used as vehicles for the recombinant generation of an array of biomolecules (*e.g.*, antibodies, PTTG proteins, etc.). Still further well-established utilities will be readily appreciated by those of skill in the art, many of which are specifically set forth in Applicants' Specification.

In fact, there are a host of specific and substantial utilities that are asserted throughout Applicants' Specification, which describes, in detail, the use of their inventive cells and the claimed method of producing them. Specifically, Applicants indicate that their inventive cells can be used to recombinantly produce PTTG proteins (*See* page 55, line 25 through page 56, line 4) as well as PTTG antibodies and "altered antibodies" (*e.g.*, chimeric antibodies, humanized antibodies, CDR-grafted antibodies, bifunctional antibodies) (*See* page 56, lines 5-16). Applicants further suggest throughout their disclosed experimental protocols that the inventive cells may be injected into a

mammal to modulate neoplastic cellular proliferation and/or transformation (*See* page 72, lines 14-16) or to examine the effects of cytotoxic anti-cancer drugs (*See* page 93, lines 12-18). The cells may also be used to generate a conditioned medium that can be used in a wide array of analytical procedures (*e.g.*, endothelial cell proliferation assays, wound migration assays, "tube forming" assays, chorio-allantoic membrane assays) (*See* page 94, lines 4-14). Taken individually or in the aggregate, Applicants' inventive cells and method of producing the same have a range of specific and substantial utilities that are particularly asserted in the Specification. Moreover, by virtue of the assertion of these utilities, Applicants respectfully point out that their claimed invention is *presumptively* useful, and that the burden is on Examiner to describe a legitimate reason why these specific and substantial utilities are insufficient.

Furthermore, while many of these asserted utilities may find application in a research setting, they do not themselves require further research to identify or confirm their utility. Certainly, Applicants' inventive cells may be the subject of further research; indeed, further study of the cells' properties may yield significant insight into the growth and development of tumors. This merely underscores the importance of Applicants' research and the tremendous impact their findings may have on the field of oncology. However, the fact that Applicants' inventive cells *can* be the subject of further study does not in any way *negate* or *lessen* the many specific and substantial utilities enumerated in the Specification. For that matter, it does not detract from the numerous well-established utilities that one of skill in the art would readily associate with the invention.

In the Office Action, Examiner succinctly concludes that Applicants' inventive cells and method of producing the same do not satisfy the utility requirement of 35 U.S.C. § 101, yet this conclusion is based entirely on an unsupported assertion that *"[t]he only readily apparent use for the method is to study the effects of the method."* Examiner does not provide any evidentiary basis whatsoever for the underlying factual assumptions, nor does he describe any reason why Applicants' asserted specific and substantial utilities would be insufficient with respect to the requirements of 35 U.S.C. § 101. He has thus failed to make a *prima facie* showing that Applicants' claimed invention lacks utility.

In light of the above remarks and the amendments to the claims, Applicants respectfully submit that their invention described in claims 32-39 and 45-52 possesses sufficient well-established

utility under 35 U.S.C. § 101, and therefore respectfully request that this rejection be reconsidered and withdrawn on that basis. In the alternative, Applicants respectfully submit that their invention described in claims 32-39 and 45-52 possesses many sufficiently asserted and credible specific and substantial utilities, and therefore respectfully request that this rejection be reconsidered and withdrawn on that basis.

In the Office Action, Examiner rejected claims 32-52 under 35 U.S.C. § 112, first paragraph, *"because the specification, while being enabling for . . . inhibiting transactivation activity of PTTG1 by nearly half via overexpression of PTTG2 protein (amino acid residues 1-191 of SEQ ID No. 64)* in vitro, *does not reasonably provide enablement for inhibiting transactivation activity of PTTG1 via overexpression of mutant PTTG2 lacking 12 C-terminal amino acid residues (residues 180-191 of SEQ ID No. 64) of the PTTG2 protein or overexpression of a mammalian PTTG2 peptide having at least 95% sequence homology with said mutant PTTG2 protein* in vitro." With respect to claims 40-44, which have been canceled by virtue of the present amendment, this rejection is rendered moot. With respect to the remaining claims, this rejection is respectfully traversed.

As amended, Applicants' independent claims 32 and 45 (from which remaining claims 33-39 and 46-52 depend, respectively) both describe the delivery of *"a first DNA segment encoding a mammalian PTTG2 peptide consisting of amino acid residues 1-191 of SEQ ID NO:64"* (emphasis added) to a mammalian cell. DNA encoding the mutant PTTG2 peptide and its homologies that were indicated as being objectionable by Examiner are no longer included within the language of these claims.

In light of the above remarks and the amendments to the claims, Applicants respectfully submit that claims 32-39 and 45-52 are adequately enabled by the Specification under 35 U.S.C. § 112, first paragraph, and therefore respectfully request that this rejection be reconsidered and withdrawn.

Applicants believe that the foregoing amendments place the application in condition for allowance, and a favorable action is respectfully requested. If for any reason Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned

attorney at the Los Angeles telephone number (213) 488-7100 to discuss the steps necessary for placing the application in condition for allowance should Examiner believe that such a telephone conference would advance prosecution of the application.

Respectfully submitted,
PILLSBURY WINTHROP LLP

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By: _____
Seth D. Levy
Registration No. 44,869
Attorney for Applicant(s)

725 South Figueroa Street, Suite 2800
Los Angeles, CA 90017
Telephone: (213) 488-7100
Facsimile: (213) 629-1033